REMARKS

Reconsideration and allowance of the subject application are respectfully requested.

By the above amendments, we have amended claims 1, 9, 10, 22 and 30 to include the limitation that the primers used in the reactions are less than 30 base pairs in length. This finds support throughout the specification, for instance, at pages 3-4. No new subject matter is added by these amendments, and entry and consideration is requested.

The May 12, 2005 Office Action is responsive to the Request for Continued Examination (RCE) and Amendment filed March 17, 2005, and the Information Disclosure Statement and cited references filed April 4, 2005.

In the Office Action, claims 1-4, 6-11 and 18-35 are rejected under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey that the inventor had possession of the claimed invention at the time the application was filed. The Examiner is arguing that the specification only describes the Bst strain 320, and does not support (1) any DNA polymerase from other species such as Bacillus caldotenax and Bacillus caldolyticus, or (2) any other DNA polymerases having 95% homology with the full length sequence of the Bst 320 DNA polymerase (as per claims 4, 18-19, 24-25, and 32-33).

We respectfully disagree. These three species—Bacillus stearothermophilis, Bacillus caldotenax and Bacillus caldolyticus—are all bacillus organisms that are known to be mesophilic in nature and very similar. We note the description in the specification at pages 15-16, and 19, which describes in some detail the use of these three mesophilic strains. The DNA polymerases of this invention are very clearly described as being moderately thermostable and derived from one of only three bacillus organisms, which DNA polymerase has proofreading 3'-5' exonuclease activity, and useful in a optimum reaction temperatures between about 45°C and about 65°C, and being rapidly inactivated above 70°C. With these specific parameters, it is not overreaching to cover DNA

polymerases having amino acid sequences that shares not less than 95% homology. In connection with this art, with our specification in hand, someone having ordinary skill in this art would recognize that the DNA polymerase of Bacillus stearothermophilis is sufficiently similar to the other mesophilic strains Bacillus caldotenax and Bacillus caldolyticus that having the DNA polymerase of the Bst 320 strain is sufficient denote "possession of the necessary common attributes or features" of the other two Bacillus strains.

In addition, the USPTO has already issued to inventor Dr. Hong et al. two U.S. patents cited by the Examiner (USP 6,165,765, cited in February 5, 2003 Office Action, and USP 6,485,909, cited in this current Office Action), which patents include claims to the three mesophilic strains and to DNA polymerases having 95% homology. The disclosures of these two issued patents have similar breadth to the instant application, at least with respect to these two points raised by the Examiner. Thus, we believe that the Examiner should be willing to permit at least the scope of these current claims.

Reconsideration is requested.

In the current Office Action, on the basis of the March 17 Amendment the Examiner has withdrawn the previous two rejections over Dr. Hong's own patent, U.S. Patent 5,834,253, and U.S. Patent 5,712,124 (Walker). However, the Examiner has made a number of new rejections, including art rejections variously combining the Iakobashvili and Lapidot (Nucleic Acids Research, 1999) reference with the inventor Dr. Hong's U.S. Patents 5,834,253, 5,747,298, and 6,485,909. That is, the Examiner has made six slightly different art rejections, all based on the same line of argument. Specifically, the rejections are as follows:

1- Claims 1-3, 6, 7 and 20 are rejected under the doctrine of obviousness-type double patenting as obvious over claims 22 and 23 of Dr. Hong's patent U.S. Patent 5,834,253 (the '253 patent) in view of Iakobachvili and Lapidot.

2- Claims 1-3, 6 and 7are rejected under the doctrine of obviousness-type double patenting as obvious over claim 6 of Dr. Hong's patent U.S. Patent 5,747,298 (the '298 patent) in view of Iakobachvili and Lapidot.

3- Claims 1-4, 6-11 and 22-35 are rejected under the doctrine of obviousness-type double patenting as obvious over claim 6 of Dr. Hong's patent U.S. Patent 6,485,909 (the '909 patent) in view of Iakobachvili and Lapidot.

4- Claims 1-4, 6-11 and 18-35 are rejected under 35 U.S.C. §103(a) as obvious over Dr. Hong's patent U.S. Patent 5,834,253 (the '253 patent) in view of Iakobachvili and Lapidot.

5- Claims 1-3, 6-10, 22 , 23 and 28-31 are rejected 35 U.S.C. §103(a) as obvious over Dr. Hong's patent U.S. Patent 5,747,298 (the '298 patent) in view of Iakobachvili and Lapidot.

6- Claims 1-4, 6-11 and 18-35 are rejected 35 U.S.C. §103(a) as obvious over Dr. Hong's patent U.S. Patent 6,485,909 (the '909 patent) in view of Iakobashvili and Lapidot.

For all of the rejections, the Examiner's rationale is basically the same: the Hong patents teach the method for enzymatic cycle primer extension reactions or direct cycle sequencing reactions using a Bst DNA polymerase, but do not teach the extension reaction temperature range of 45°-65° or a melting temperature of about 70° or an annealing temperature of about 37°. The Iakobashvili and Lapidot reference is cited to make up the deficiency of the Hong patents, by allegedly teaching these temperature ranges.

However, the Iakobashvili and Lapidot reference is itself easily distinguished from our invention. In our specification on pages 3-4, this references is discussed as follows:

> Lowering the glycerol concentration to17 % (v/v) in the reaction mixture with the addition of proline appeared to protect the Klenow polymerase activity in cycle PCR at the temperature range between 70°C and 37°C. (Iakobashvili and Lapidot) Significantly, neither of these procedures for low temperature cycle primer extension has been shown to generate high quality sequence-specific PCR products, or has been shown to generate reaction products suitable for DNA sequencing. In the Iakobashvili and Lapidot report, the PCR products generated in low-temperature cycle primer extension have not proved to be sequence-specific, especially when primers of 20-25 base pairs (bp) in length were used. Although the application was said to be successful for cycle extension of long primers (such

as 30-35 bp in length) using the Klenow polymerase at the low temperature range, the system has not been shown to generate useful sequence-specific amplification products from such long primers. Since most primers used for DNA cycle sequencing and for PCR are shorter than 30 bp in length, there is a need for a low-temperature cycling system with which sequence-specific extension of primers of shorter than 30 bp (preferably about 20 bp) can be achieved to generate useful amplification DNA products for sequencing and for further molecular analysis.

To further clarify our invention, we have amended the claims above to specify that the primers used are less than 30 base pairs in length. This clearly distinguishes our invention from anything taught or suggested by Iakobashvili and Lapidot. Withdrawal of these rejections is respectfully requested.

Turning to another matter, on page 16, the Examiner has stated his claim interpretation of the term "about" with respect to "about 10% and about 20% glycerol", "about 70°C" for the melting temperature, and "about 37° C" for the annealing temperature. In particular, the Examiner states: "the term 'about' is broader in scope and can include any number around the given range of temperature or concentration of glycerol. Further the instant claims recite annealing temperature of about 37°C, which supports the range recited in the preamble is broader by +/- 10° C." We object to this interpretation, as it is not what the applicant intended when the application was filed. This interpretation seems unreasonable—someone having ordinary skill in this art would readily understand that these temperatures and concentrations cannot include "any number around" them, especially in light of the description in the examples and specification. The term "about" is simply a recognition that much in science is imprecise, and cannot be quantified with precision. This is acknowledged in all of science. For instance, certainly someone having ordinary skill in this art, with our disclosure in hand, would understand that "about 70°C" melting temperature does not encompass 80°C—especially, since our specification makes clear that the DNA polymerases are rapidly inactivated at temperatures above 70°C.

In summary, all of the Examiner's outstanding rejections and objections have been addressed, and the application is believed to be in allowable form. Notice to that effect is earnestly solicited. No amendment made was related to the statutory

requirements of patentability unless expressly stated herein, and no amendment made was for the purpose of narrowing the scope of any claim unless we argued above that such amendment was made to distinguish over a particular reference or combination of references.

If the Examiner has any questions or would like to make suggestions as to claim language, the Examiner is encouraged to contact Marlana K. Titus at (301) 977-7227.

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